MEMORANDUM

To: Joshua Lederberg
Subject: Your memo and inquiries of September 22, 1972 regarding Avery and Griffith.
Date: September 28, 1972
From: Al Coburn

1. "Conceptual antecedents that may have inspired his experiments". Griffith was wedded to bacteria and fascinated with their behavior. In 1928 "bacterial variation" was a naughty word. Nevertheless, the concept intrigued some who saw it. For example, during April 1928 I ran into it when a colony of Staph. Aureus blew in the window of the brand new lab. on "G" Floor of P. and S. Dochez was startled and took one blood agar plate of my strep. variant home, saying "Avery will be interested in this". By coincidence that lab. was soon to be devoted for a decade to the studies of transforming the pneumococcus by Martin Henry Dawson et al.

It was also about 1928 that Dochez conceived that the bacterial flora of the chimpanzee pharynx produced variants when filterable viruses from persons with "common cold" were introduced into the naso pharynx of the chimp.

As for the inspiration for Griffith's experiments there were at least two antecedents. Griffith was curious about this phenomenon of variation. Was it true or merely an artifact, as most bacteriologists believed in the early 'twenties? He no doubt realized that his 1929 findings would not be accepted by his "peers" and so probably never referred to this work, certainly not in the literature or to me.

But curiosity was perhaps the minor motivation. The major motivation, as I learned when I too became enamoured, much later, was his fascination with the epidemiology of beta hemolytic streptococcus. As W. Hayes pointed out, in the First Griffith Memorial Lecture (see enclosed), "He believed that a proper understanding of epidemiologic problems could come only from more detailed and discriminating knowledge of infectious bacterial species and of the nature of bacterial virulence and variation". This deep interest of Griffith I did not learn until I too had become intrigued with variants that had what I chose to call "infectivity for the respiratory tract of man" rather than "virulence for the mouse". There is no doubt in my mind that Griffith saw all of this clearly and that this was the "conceptual antecedent" to his colossal task of identifying hemolytic streptococcus serologically by his slide agglutination method of typing. Whereas the sporadic infection was drab, the sudden outburst of a streptococcal epidemic was an alluring challenge. There is no doubt in my mind that Griffith, the bachelor, was inspired by the romance of a concept, i.e. one variant of Streptococcus pyogenes with great "infectivity" (commonly called virulence) for man could produce a devastating

epidemic. And believe me when one is inspired with this concept all other matters seem momentarily insignificant.

After this Englishman of few papers published his pneumococcal findings, he felt that he had done his thing and had no stomach to become involved in controversy. He closed the book and let posterity be the judge while he concentrated on matters epidemiological. Whether he corresponded with Avery about the pneumococcus I never asked and do not know. Avery regarded Griffith so highly that he accepted his findings(and may have been the only person so to do). Accordingly, Avery devoted the succeeding decades of his life to its elucidation. In this connection, there may be correspondence on this point; so I enclose a copy of a letter from Avery's sister-in-law. Please note the postscript. At least I have expressed my guess that you requested on the "conceptual antecedents".

2. "Further recollections about the impact" etc. First, let me state that for many years I knew no geneticists. In fact, I knew only the name of one in New York. His daughter, who worked at the Rockefeller Institute wore a magnificent, fawn colored gabardine suit! Between 1942 and 1946 I was on active duty in the Navy. But one recollection remains permanent. Avery presented at the Rockefeller's Friday afternoon conference his information on DNA as the transforming factor. On that occasion, a certain capable chemist-biologist attacked Avery with such vehemence that it sent Charlie Hoagland and me into a tailspin. The antagonist was not a geneticist. In fact, I do not believe that the Rockefeller Institute had any geneticists in its ranks during that era. But it did have nucleic acid chemists of great renown.

3. "Overlooked by most of his peers". Let me try to clarify this puzzlement. When I wrote overlooked by most of his distinguished peers, I was unhappy with the word peer - defined in my Webster's Seventh Intercollegiate Dictionary as "one that is of equal standing with another". Theoretically, all full Members of the Rockefeller Institute were of equal standing, and actually many of these Members were considered distinguished persons. But how many of them did <u>not</u> overlook the significance of Avery's contribution? I know of only two, the elderly Rufus Cole and the youthful Charles Hoagland. Wendell M. Stanley, working at the R. I. in Princeton did more than overlook. In 1970 he finally published his apology.

I certainly did <u>not</u> mean, even to suggest, that Avery should have been awarded a Nobel Prize. I know nothing about qualifications for this great honor. Like F. Gowland Hopkins, Avery seemed above the hierarchy of the "Nobellates" or any other research physician.* In fact, I now wonder whether Avery had only one American peer as a biologist, Theobald Smith. A couple of years ago Dickinson W. Richards mentioned to me the name of the scientist (chemist, as I recall) who served the Nobel Committee as Avery's blocking agent. Perhaps that is the answer to your question as to "why Avery was not en-Nobelled

* of my acquaintance

much earlier for his work in immunochemistry". My travels in simple, clinical medical research circles have not taken me into the rarefied atmosphere of those recognized as top notch scientists.

4. "Had Avery done his DNA work in his 50's he of course could not have been ignored". On this point may I be the devil's advocate? Avery worked on the transforming factor from age 51 until compulsory retirement. Even then he obtained as assistant, a female geneticist, since help from this discipline was not available at R. I. It was not until she had to leave (? for marriage) that Avery told me he felt that he had gone as far as he could, with his lack of training in genetics, was closing up the shop and moving South to become a neighbor of his brother Roy in Nashville. Your statement, "he just did not live long enough thereafter" brings two memories; (a) Tiselius gave the same excuse, (b) in congratulating Nobel Laureate, F. Peyton Rous, I told him that perhaps more important than doing his cancer work as a young man was his ability to live into senescence. There was no rebuttal, but a postcard* of thanks. At that time, and only at that late date, Rous told me that Avery should have received a Nobel Medal. It is a matter of record that Avery did live in good health until 1955, twelve years after publishing his work on DNA as the transforming factor. But perhaps you meant to indicate that it would have taken more than twelve years for Arne Tiselius to get the message!

It seems to me that I will not receive a passing grade in attempting to answer your questions. If ever I have the privelege of meeting you, there is one question, as indicated by the remarks about Avery, on my mind: Are there men whose thinking and whose fruits of labor transcend the ability of their contemporaries to evaluate accurately the significance of their discoveries? I once asked this question of Dick Richards. His prompt reply was that after all distinguished scientists were only human.

I close this by attaching a snapshot of Avery taken in March of 1943. Avery because of his solemnity was long considered old and was called "Professor" when he was a young man. Photographs make him appear worried. Perhaps he always was overwhelmed by his responsibilities until the spring of 1943. You will note from this poor snapshot that Avery has a happy smile. He had nailed down DNA for the world to study. At long last he was pleased. What a man!

Thank you for your inquiries.

Alvin F. Coburn M. D.

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* selected at the British Museum by Mrs. Rous